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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/613,105

07/02/2003

Luca Rastelli

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02/28/2006

EXAMINER

ASHEN, JON BENJAMIN

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ART UNIT

PAPER NUMBER

1635

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/613,105	Applicant(s) RASTELLI ET AL.	
	Examiner Jon B. Ashen	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/03</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Status of the Application

1. Claims 1-8 are pending and currently under examination in this Application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 4 recite, "a) measuring expression of a nucleic acid encoding an antileukoprotease polypeptide in a test sample; and b) comparing the expression of the nucleic acid in the test sample to the expression of a nucleic acid encoding an antileukoprotease polypeptide in a cancer reference profile,...". However, the skilled artisan cannot determine the metes and bounds of what is being claimed with this terminology, without assumption, because as written, only one nucleic acid ("a nucleic acid encoding an antileukoprotease polypeptide in a test sample") has antecedent basis and the claim requires comparing the expression of that nucleic acid to "the nucleic acid in the test sample." Claims 2-4 and 5-8 are rejected due to their dependence on a rejected claim.

4. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention. The term "similarity" in claims 1 and 4 is a relative term which renders the claim indefinite. The term "similarity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The skilled artisan cannot determine, without assumption, the metes and bounds of what would constitute a similarity between the expression of the nucleic acid in the test sample and the expression of a nucleic acid encoding antileukoprotease in a cancer or reference profile, as claimed.

5. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 recites, "wherein the nucleic acid encoding an antileukoprotease polypeptide comprises the amino acid sequence of SEQ ID NO: 2." However, the skilled artisan cannot determine the metes and bounds of what is being claimed with this terminology, without assumption, because nucleic acids that encode polypeptides comprise nucleotides, but do not comprise amino acids. Deletion of the word, "comprises" and replacement with the text, "encodes," or deletion of the "nucleic acid encoding an," would be remedial.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-2 and 4-5 are drawn to a method of identifying a cancer cell by measuring the expression of a nucleic acid encoding an antileukoprotease polypeptide in a test sample and comparing to a reference sample that is a cancer reference profile or a normal reference profile wherein the cancer can be ovarian, thyroid or renal wherein the nucleic acid comprises the sequence of SEQ ID NO: 1 and wherein the nucleic acid encoding an antileukoprotease polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

Instant claims 1-2 and 4-5 are broadly drawn and read on a method of identifying a cancer cell that can be any cancer cell by measuring expression of an antileukoprotease polynucleotide. Additionally, instant claims 1-6 read on the method above wherein the nucleic acid encoding an antileukoprotease polypeptide is any nucleic acid encoding any antileukoprotease polypeptide from any organism.

However, the specification as filed does not provide an adequate written description of the instantly claimed methods because the specification does not adequately describe a representative number of species from within the broad genus of methods that function, commensurate with the breadth of what is claimed, to identify any cancer cells from any organism by based on the "similarity" between the expression

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of an antileukoprotease nucleic acid and the total expression of the nucleic acid in the test sample.

The specification discloses that the expression pattern of antileukoprotease nucleic acid is unregulated in certain species of cancer and lung cells and that antileukoprotease is unregulated in species of thyroid, ovarian and kidney tumors and cell lines (pg. 3). The specification discloses the comparison of antileukoprotease expression levels in test cell populations vs. cancer and normal reference cell populations and the results (pg. 19, tables 3-4) of antileukoprotease nucleic acid expression profiles from different cell types. The tables provide some evidence of the up regulation of antileukoprotease nucleic acid expression in ovarian cancer cells but no consistent indication or correlation of the expression levels of antileukoprotease nucleic acid in other cancers, including those not listed or tested, that would indicate that Applicant was in possession of the instant method of identifying any cancer cell, commensurate with the breadth of what is now claimed. The specification provides no definition of what constitutes "similarity" between the expression of a nucleic acid and the nucleic acids in a reference expression profile that would indicate that applicant was in possession of a broad genus of method that functions to identify a cancer cell based on that "similarity", as claimed.

The specification provides no examples of the broad genus of methods as claimed (i.e., no disclosure of any cancer cells of any type that are actually identified). The specification provides only a general disclosure, as above, of the expression levels of antileukoprotease nucleic acid in several different types of cancer and non-cancer

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cells. In this regard, the specification is prophetic and does not provide a correlation between the structure of the nucleic acid encoding antileukoprotease polypeptide and the function of being expressed in any cancer cell such that any cancer cell could be identified by the level of expression of this nucleic acid. Additionally, the specification has not disclosed any distinguishing identifying characteristics of the broad genus of claimed methods that would function, commensurate with the breadth of what is claimed. The measurement of the expression of an antileukoprotease nucleic acid from a test sample is not considered a distinguishing identifying characteristic of the genus because there is no indication, in the specification or the prior art (see below), that the expression of this nucleic acid can be used to identify any cancer cell with any type of cancer from any organism, including cancers yet to be described or studied in detail and those cancers wherein the expression levels of antileukoprotease is invariant.

The general disclosure of the specification, therefore, fails to provide an adequate written description of the broad genus of methods that function, commensurate with what is claimed. The specification does not provide an adequate written description such that one of skill in the art, at the time the instant invention was made, would be reasonably led to the instant invention or that would allow the skilled artisan to recognize that Applicant was in possession of the instant invention, commensurate with the breadth of what is claimed. The state of the art cannot provide the required description because it is silent with regards to the expression of antileukoprotease in cancer cells. This is evidenced by Sallenave 2000 (Respir. Res. Vol. 1, 87-92), who review of the role of antileukoprotease in disease in general and

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specifically in inflammatory lung disease and who are silent with regards to the expression of antileukoprotease nucleic acid in cancer cells.

MPEP § 2163[R-2] I. states:

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., > Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); < Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

The fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc., 935 F.2d at 1563-64, 19 USPQ2d at 1117.

Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. > Enzo Biochem, 323 F.3d at 964, 63 USPQ2d at 1613.<

In the instant case, Applicant has not provided adequate written description of their invention because the specification does not convey, with reasonable clarity to those of skill in the art, as of the filing date sought, that applicant was in possession of the invention now claimed.

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8. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an method of identifying an ovarian cancer cell comprising comparing the expression of a nucleic acid encoding antileukoprotease polypeptide with a reference expression profile of a nucleic acid encoding antileukoprotease polypeptide (either a normal reference profile or a cancerous reference profile), does not reasonably provide enablement for the full scope of what is claimed, which is a method of identifying any cancer cell having any type of cancer by comparing the expression profiles of antileukoprotease nucleic acid between test and reference samples, as above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. as failing to comply with the enablement requirement.

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

In the instant case, the specification does not provide an adequate written description of the broad genus of methods as claimed (see above). Therefore, absent this written description, the skilled artisan would be required to perform vast quantities

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of *de novo* undue trial and error experimentation in order to both make and use the method as claimed, based on the content of the disclosure, to identify any cancer cell that could be any type of cancer cell beyond an ovarian cancer cell. The state of the art, as shown by Sallenave (set forth in the previous rejection), is silent with regards to the breadth of cancer cells wherein antileukoprotease nucleic acid expression differs from that of non-cancerous cells. Thus, one of skill in the art could not practice the invention commensurate in scope with the claims without undue, *de novo* trial and error experimentation in order to determine, at least, in which, of all cancer cells, antileukoprotease nucleic acid expression varies from that observed in the same type of non-cancerous cell, such that a person skilled in the art to which it pertains would be enabled for a method of identifying any cancer cell having any type of cancer, as claimed. Additionally, the type of experimentation required to practice the invention more broadly that is exemplified is a factor in the enablement analysis, but is not dispositive. In this case, even if the nature of each experiment required to expand the scope of the enabled invention was considered standard (which it is not), it would be outweighed by the sheer quantity of experimentation required to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Brien et al. (US 6,602,674) (which is supported by the disclosure of US Provisional Application 60/159,9762). The invention set forth in claims 1-6 is drawn to a method of identifying a cancer cell by measuring the expression of a nucleic acid encoding an antileukoprotease polypeptide in a test sample and comparing to a reference sample that is a cancer reference profile (claim 1) or a normal reference profile (claim 4) wherein the cancer can be ovarian, thyroid or renal (claims 2 and 5) or is ovarian (claims 3 and 6).

O'Brien et al. disclose a method of measuring the expression of a nucleic acid encoding an antileukoprotease polypeptide in test samples of ovarian cancer and provide tables which compare the expression of a nucleic acid encoding an antileukoprotease polypeptide in the test samples of ovarian cancer with the expression profiles of antileukoprotease nucleic acid from both normal and cancerous cells, thereby identifying cancer cells that have ovarian cancer (see cols. 2, 4 and Tables 1 and 2).

Therefore, the instant invention as set forth in claims 1-6 is anticipated by O'Brien.

11. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Au-Young et al. (US 6,500,938). The invention set forth in claims 1-6 is relied upon as

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above. The invention set forth in claims 7 and 8 is drawn to the method above wherein the nucleic acid comprises SEQ ID NO: 1 or wherein the nucleic acid encoding an antileukoprotease polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

In the instant case, although claim 8 is considered indefinite for the reasons set forth above, prior art is applied in the interests of compact prosecution and is based on the reasonable interpretation that claim 8 reads on the method above wherein the antileukoprotease polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

Au-Young et al. disclose SEQ ID NO: 1024 that is identical to instantly claimed SEQ ID NO: 1, that is the human mRNA for antileukoprotease (ALP) from cervix uterus (cols. 57-58) (see also attached sequence alignment). Au-Young et al. disclose that the sequences of their invention can be used on a microarray or as hybridization probes in methods of expression profiling, in order to catalogue differences in gene expression between healthy and diseased tissues or cells (col. 11). Au-Young et al. disclose the use of expression profiling to diagnose cancer, including ovarian cancer (cols. 11-12), which is considered. The disclosures of Au-Young et al. are reasonably considered to anticipate the instantly claimed invention because they disclose nucleic acid expression profiles that can be generated with the hybridization probe of their invention, including SEQ ID NO: 1024 would be compared, inherently, from healthy and diseased tissues or cells, in order to catalogue differences in gene expression and to diagnose cancer including ovarian cancer.

Therefore, Au-Young et al. anticipate the instant invention as set forth in claims 1-8.

12. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Morin et al. (US 2003/0211498) (which claims priority from US Provisional Application 60/194,336). The invention set forth in claims 1-8 and the interpretation of claim 8 for the purposes of compact prosecution and prior art are relied upon as above.

Morin et al. disclose methods of detecting ovarian cancer in a subject by comparison of the expression of tumor marker genes between samples taken from the subject and normal and cancer reference profiles (pg. 1, [0005-0013]). Morin et al. disclose SEQ ID NO: 53 that is an ovarian cancer tumor marker that is identical to instantly claimed SEQ ID NO: 1, that is the mRNA encoding secretory leukocyte protease inhibitor (which is also known as antileukoprotease) (pg. 2, [0023]; pg. 4, [0053]) (see also, attached sequence alignment).

Therefore, Morin et al. anticipate the instant invention as set forth in claims 1-8.

Conclusion

13. No claims are allowed.

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15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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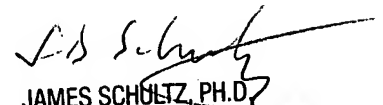
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Jba


JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER